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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,320	01/31/2002	Jonathan S. Stamler	1818.1030-003	1921

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BOSTON, MA 02111

EXAMINER
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GUPTA, ANISH

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 11/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

10/066,320

Applicant(s)

STAMLER ET AL.

Examiner

Anish Gupta

Art Unit

1654

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 27 September 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE:

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 30-35.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

  
**ANISH GUPTA**  
**PRIMARY EXAMINER**

Continuation of 11. does NOT place the application in condition for allowance because: The claims remain rejected for the reasons set forth in the previous office actions and the reasons set forth below.

Applicants assert that the specification describes low phosphate conditions result in cooperatively of NO binding and high yield of SNO formation. "Experiments described in Example 3 were designed to measure the yield of iron nitrosylhemoglobin vs. metHb under low phosphate conditions. . .not to measure the yield of SNOHb under those conditions." The experiments in Example 4 were designed to measure the yield of SNOHb and those results show that SNOHb and intraerythrocytic SNOHb are produced under those low phosphate conditions.

Applicants arguments have been fully considered but have not been found persuasive.

While the reasons for conducting the experiments may have been as Applicants describe, the results cannot be overlooked. The claims call of "conditions." The results of the experiments show that not all conditions, even under low phosphate, result in the desired product. As stated in the previous office actions, the results indicate that when 100 mM phosphate was used, formation of metHb was observed. Using 10mM phosphate shows the formation of iron nitrosyl Hb and some metHb. Using 10mM phosphate + borate resulted in predominantly iron nitrosylHb. Thus when phosphate is present in a concentration of 10mM the desired S-nitrosylHb is not obtained, rather Fe-nitrosylHb is obtained (see page 46 of Jia). Even where the phosphate concentration is in the range of 10 mM, much like the concentration claimed in claim 31, S-nitrosylHb is not obtained rather Fe-nitrosylHb is obtained. Clearly, "low concentrations" of phosphate is not enough to produce the desired product. Accordingly, specific conditions are necessary to make desired end product. The instant specification does not describe the all of the desired conditions to achieve S-nitrosohemoglobin. One would be burdened with undue experimentation in determining the appropriate conditions for obtaining S-nitrosylhemoglobin rather than obtaining methemoglobin or iron-nitrosylhemoglobin. .